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Supplemental Materials regarding to the article submitted to Twin Research and Human Genetics

Exposure to air pollution from traffic and neurodevelopmental disorders in Swedish Twins

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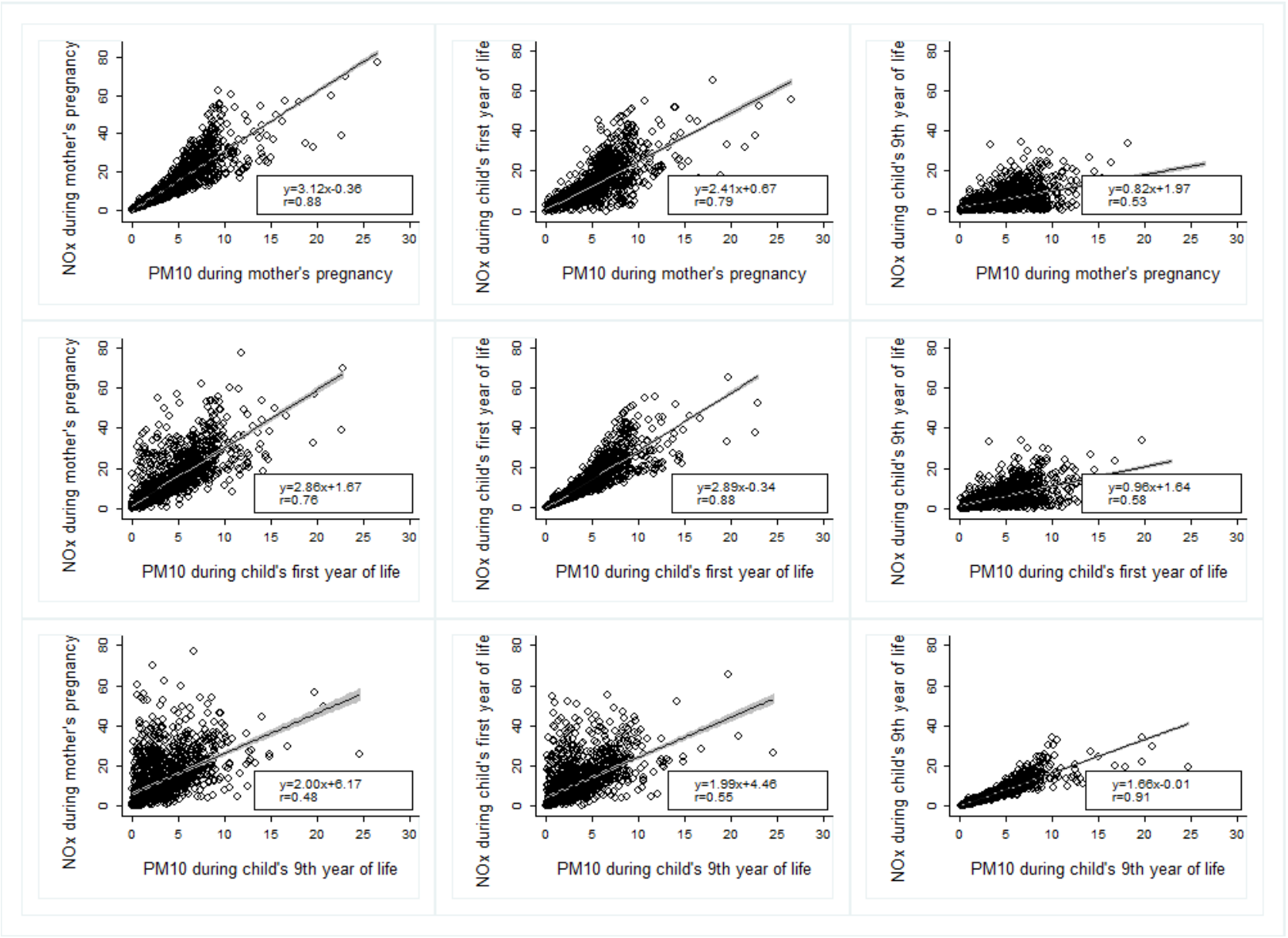

Figure S1b. Correlation of each pollutant (NO_x and PM_{10} in $\mu g/m^3$) over different study periods (n=3,408 for child's first year of life; n=3,041 for child's 9th year of life)

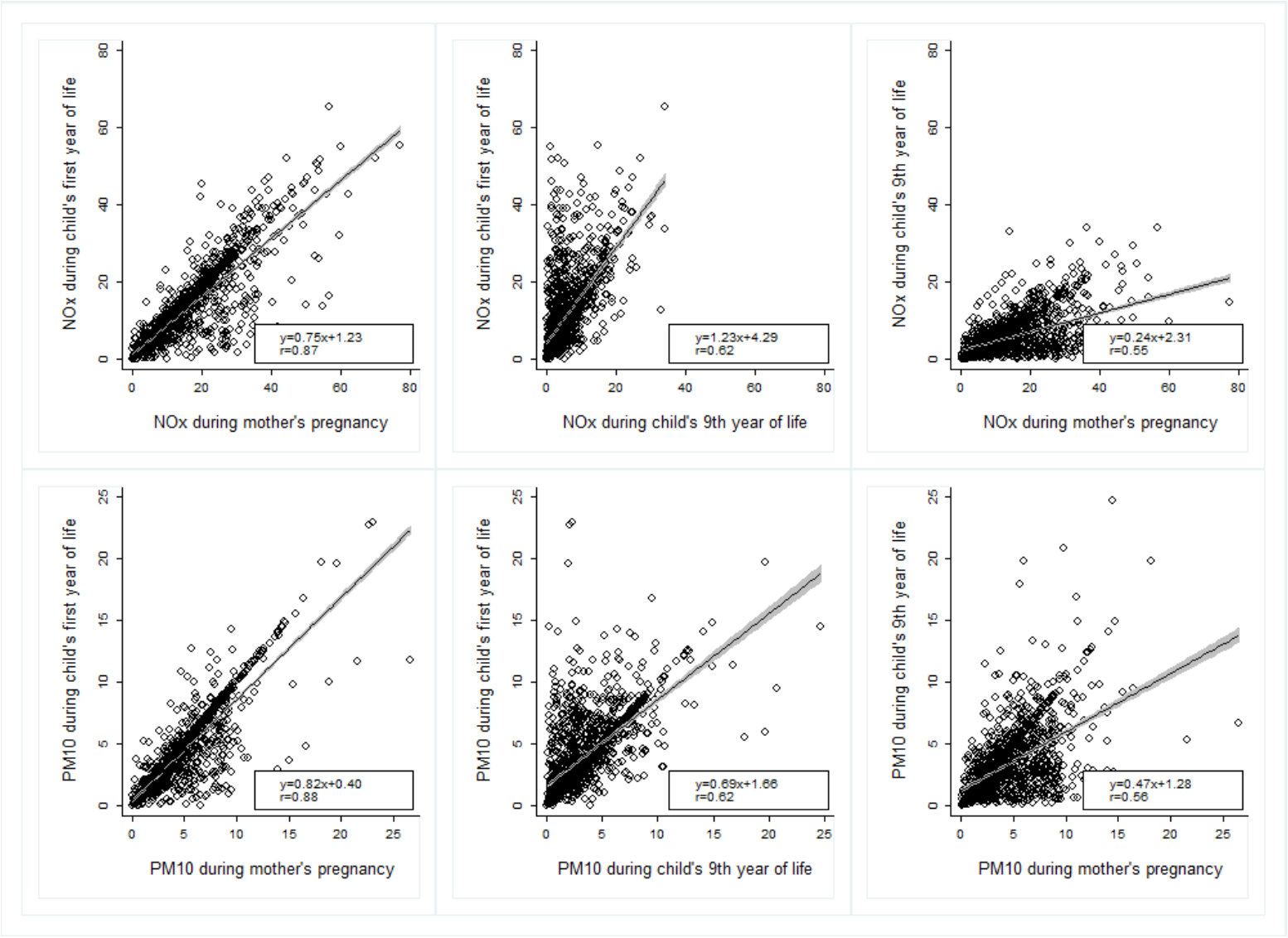

Table S1. Codes based on the 9th and 10th edition of International Classification of Diseases (ICD-9 and ICD-10) used to identify cases with chromosome abnormalities, neural tube defects and other neurological diseases from the National Patient Register and the telephone interview.

Diseases	ICD-9 codes	ICD-10 codes	N
Down's syndrome	758A	Q90	4
Fragile X syndrome	759.8 or 759W	Q99.2	0
Other chromosome aberrations	758B,C,D,E,F,G,H,W, X	Q91-Q92	0
Epilepsy	345	G40-G41	25
Spina bifida and other congenital anomalities of nervous system	741,742	Q01-Q07	4
Mental retardation	317, 318, 319	F70-F79, F88-F89	74
Cerebral paresis and plegias	342, 343, 344	G80, G81-G83	24
Other neurological disorders	330, 333-337, 348-349, 434, 436- 437	G90-G99	9

Table S2. Distribution of NO_x and PM_{10} exposure levels for different trimesters during pregnancy

	10th percentile	25th percentile	Mean	Median	75th percentile	90th percentile	Missing (n)
First trimester							
NO_x exposure ($\mu g/m^3$)							
Dispersion model	2.53	4.94	13.27	9.25	18.78	29.76	105
Dispersion model with seasonal variation but no imputation	2.50	4.61	12.33	8.59	17.62	27.83	1,035
Dispersion model with seasonal variation and imputation	2.62	5.02	13.26	9.33	18.61	30.21	105
PM_{10} exposure ($\mu g/m^3$)							
Dispersion model	0.95	1.94	4.28	3.42	6.15	8.50	105
Dispersion model with seasonal variation but no imputation	0.19	1.62	4.29	3.62	6.48	9.18	1,196
Dispersion model with seasonal variation and imputation	0.18	1.58	4.32	3.78	6.62	9.18	1,001
Second trimester							
NO_x exposure ($\mu g/m^3$)							
Dispersion model	2.49	4.74	12.76	9.00	18.01	28.42	80
Dispersion model with seasonal variation but no imputation	2.20	4.46	11.95	8.65	16.81	26.86	865
Dispersion model with seasonal variation and imputation	2.31	4.72	12.73	8.99	17.68	28.38	80
PM_{10} exposure ($\mu g/m^3$)							
Dispersion model	0.95	1.90	4.22	3.36	5.98	8.45	80
Dispersion model with seasonal variation but no imputation	0.28	1.75	4.22	3.66	6.24	8.81	994

Dispersion model with seasonal variation and imputation	0.48	1.73	4.26	3.68	6.23	8.80	834
Third trimester							
NO_x exposure ($\mu g/m^3$)							
Dispersion model	2.42	4.67	12.03	8.38	16.37	26.95	100
Dispersion model with seasonal variation but no imputation	2.06	4.24	11.37	8.06	15.57	25.18	812
Dispersion model with seasonal variation and imputation	2.11	4.59	12.03	8.60	16.55	26.73	100
PM_{10} exposure ($\mu g/m^3$)							
Dispersion model	0.92	1.86	4.09	3.24	5.80	8.32	100
Dispersion model with seasonal variation but no imputation	-0.19	1.54	4.14	3.67	6.27	8.91	1,000
Dispersion model with seasonal variation and imputation	0.03	1.57	4.19	3.69	6.29	8.87	794

Table S3a. Crude and adjusted ORs of neurodevelopmental disorders for twins born in Stockholm, by exposure to NO_x in each trimester

Outcomes	Case	NO_x during 1st trimester		NO_x during 2nd trimester		NO_x during 3rd trimester	
		OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
ASD							
ASD_{low}	109	0.96 (0.48,1.95)	0.96 (0.47,1.99)	0.91 (0.43,1.95)	0.88 (0.40,1.93)	0.90 (0.41,1.99)	0.99 (0.46,2.14)
ASD_{high}	33	0.58 (0.21, 1.62)	0.72 (0.25, 2.10)	0.33 (0.10, 1.02)	0.43 (0.13, 1.41)	0.37 (0.12, 1.13)	0.47 (0.13, 1.74)
ASD_{DSM-IV}	47	0.78 (0.30,2.06)	0.85 (0.33,2.22)	0.58 (0.19,1.75)	0.61 (0.20,1.83)	0.67 (0.22,2.05)	0.74 (0.23,2.38)
ADHD							
$ADHD_{low}$	328	0.70 (0.46,1.06)	0.84 (0.54,1.29)	0.76 (0.49,1.18)	0.89 (0.57,1.39)	0.86 (0.56,1.34)	1.03 (0.67,1.60)
$ADHD_{high}$	62	0.59 (0.21,1.61)	0.74 (0.30, 1.84)	0.49 (0.17,1.45)	0.61 (0.23,1.63)	0.57 (0.19,1.69)	0.68 (0.25, 1.88)
$ADHD_{DSM-IV}$	152	0.52 (0.27,1.00)	0.59 (0.31,1.13)	0.58 (0.30,1.13)	0.62 (0.33,1.19)	0.67 (0.35,1.29)	0.77 (0.41,1.45)
Any neurodevelopmental outcomes							
ASD or ADHD	355	0.75 (0.50, 1.13)	0.88 (0.58, 1.33)	0.81 (0.54, 1.23)	0.92 (0.60, 1.41)	0.90 (0.60, 1.37)	1.07 (0.70, 1.62)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.

Table S3b. Crude and adjusted ORs of neurodevelopmental disorders for twins born in Stockholm, by exposure to PM_{10} in each trimester

Outcomes	Case	PM_{10} during 1st trimester OR[a] (95% CI)	PM_{10} during 1st trimester OR[b] (95% CI)	PM_{10} during 2nd trimester OR[a] (95% CI)	PM_{10} during 2nd trimester OR[b] (95% CI)	PM_{10} during 3rd trimester OR[a] (95% CI)	PM_{10} during 3rd trimester OR[b] (95% CI)
ASD							
ASD_{low}	109	0.96 (0.49,1.89)	1.05 (0.54,2.01)	0.93 (0.45,1.92)	0.96 (0.49,1.90)	1.02 (0.48,2.13)	1.11 (0.57,2.17)
ASD_{high}	33	0.71 (0.30, 1.72)	0.88 (0.36, 2.16)	0.48 (0.17, 1.39)	0.62 (0.22, 1.71)	0.55 (0.18, 1.65)	0.70 (0.23, 2.20)
ASD_{DSM-IV}	47	0.83 (0.39,1.78)	0.85 (0.43,1.69)	0.66 (0.28,1.56)	0.65 (0.31,1.39)	0.74 (0.31,1.78)	0.73 (0.33,1.62)
ADHD							
$ADHD_{low}$	328	0.77 (0.52,1.14)	0.93 (0.63,1.38)	0.84 (0.56,1.24)	0.97 (0.66,1.43)	0.93 (0.63,1.38)	1.12 (0.77,1.63)
$ADHD_{high}$	62	0.55 (0.25,1.22)	0.70 (0.35,1.41)	0.49 (0.21,1.15)	0.62 (0.30,1.28)	0.52 (0.22,1.25)	0.62 (0.29,1.36)
$ADHD_{DSM-IV}$	152	0.70 (0.38,1.26)	0.78 (0.45,1.36)	0.80 (0.43,1.47)	0.85 (0.49,1.49)	0.86 (0.47,1.57)	0.97 (0.56,1.68)
Any neurodevelopmental outcomes							
ASD or ADHD	355	0.81 (0.56, 1.17)	0.96 (0.66, 1.40)	0.86 (0.59, 1.25)	0.99 (0.68, 1.43)	0.96 (0.66, 1.39)	1.13 (0.79, 1.63)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.

Table S4a. Sensitivity analyses: crude and adjusted ORs of neurodevelopmental disorders for twins born in Stockholm, by exposure to NO_x in each trimester with seasonal variation

Outcomes	Case*	NO_x during 1st trimester OR[a] (95% CI)	NO_x during 1st trimester OR[b] (95% CI)	NO_x during 2nd trimester OR[a] (95% CI)	NO_x during 2nd trimester OR[b] (95% CI)	NO_x during 3rd trimester OR[a] (95% CI)	NO_x during 3rd trimester OR[b] (95% CI)
ASD							
ASD_{low}	96	0.96 (0.47,1.96)	0.95 (0.46,1.98)	0.91 (0.43,1.92)	0.87 (0.40,1.89)	0.89 (0.40,2.00)	0.97 (0.44,2.17)
ASD_{high}	29	0.61 (0.23, 1.65)	0.78 (0.30, 2.05)	0.33 (0.11, 1.04)	0.43 (0.13, 1.37)	0.34 (0.10, 1.16)	0.42 (0.10, 1.84)
ASD_{DSM-IV}	43	0.81 (0.31,2.10)	0.89 (0.35,2.26)	0.55 (0.18,1.67)	0.57 (0.19,1.70)	0.64 (0.20,2.06)	0.68 (0.19,2.41)
ADHD							
$ADHD_{low}$	303	0.70 (0.45,1.07)	0.84 (0.54,1.31)	0.75 (0.49,1.16)	0.87 (0.56,1.36)	0.85 (0.54,1.33)	1.02 (0.65,1.60)
$ADHD_{high}$	56	0.57 (0.20,1.59)	0.72 (0.28, 1.84)	0.47 (0.16,1.40)	0.58 (0.21,1.58)	0.59 (0.20,1.74)	0.70 (0.25, 1.95)
$ADHD_{DSM-IV}$	140	0.50 (0.25,0.98)	0.57 (0.29,1.11)	0.57 (0.29,1.11)	0.61 (0.32,1.17)	0.69 (0.36,1.33)	0.79 (0.42,1.50)
Any neurodevelopmental outcomes							
ASD or ADHD	328	0.76 (0.50, 1.14)	0.88 (0.58, 1.34)	0.81 (0.53, 1.22)	0.91 (0.60, 1.39)	0.89 (0.58, 1.36)	1.05 (0.68, 1.62)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

*Case: Number of cases identified among twins with non-missing values (after imputation) for NO_x exposure.

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.

Table S4b. Sensitivity analyses: crude and adjusted ORs of neurodevelopmental disorders for twins born in Stockholm, by exposure to PM_{10} in each trimester with seasonal variation

Outcomes	Case*	PM_{10} during 1st trimester OR[a] (95% CI)	PM_{10} during 1st trimester OR[b] (95% CI)	PM_{10} during 2nd trimester OR[a] (95% CI)	PM_{10} during 2nd trimester OR[b] (95% CI)	PM_{10} during 3rd trimester OR[a] (95% CI)	PM_{10} during 3rd trimester OR[b] (95% CI)
ASD							
ASD_{low}	75	0.87 (0.38,2.01)	0.98 (0.46,2.09)	0.77 (0.30,1.97)	0.87 (0.37,2.04)	0.80 (0.31,2.10)	0.78 (0.31,1.95)
ASD_{high}	25	0.81 (0.37, 1.79)	0.99 (0.42, 2.36)	0.60 (0.23, 1.53)	0.84 (0.39, 1.78)	0.31 (0.10, 0.99)	-
ASD_{DSM-IV}	33	0.87 (0.41,1.87)	0.98 (0.45,2.11)	0.65 (0.27,1.55)	0.66 (0.31,1.39)	0.47 (0.18,1.19)	0.29 (0.10,0.84)
ADHD							
$ADHD_{low}$	225	0.81 (0.50,1.31)	0.92 (0.58,1.47)	0.84 (0.54,1.32)	1.12 (0.72,1.72)	0.96 (0.61,1.52)	1.02 (0.65,1.62)
$ADHD_{high}$	47	0.36 (0.15,0.88)	0.48 (0.20,1.15)	0.37 (0.16,0.89)	0.54 (0.24,1.21)	0.28 (0.09,0.91)	0.32 (0.10,1.00)
$ADHD_{DSM-IV}$	106	0.58 (0.28,1.18)	0.67 (0.35,1.29)	0.67 (0.34,1.34)	0.87 (0.47,1.60)	0.83 (0.40,1.70)	0.87 (0.44,1.72)
Any neurodevelopmental outcomes							
ASD or ADHD	242	0.83 (0.53, 1.30)	0.95 (0.61, 1.48)	0.85 (0.55, 1.31)	1.11 (0.73, 1.70)	0.97 (0.62, 1.50)	1.02 (0.65, 1.59)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

*Case: Number of cases identified among twins with non-missing values (after imputation) for PM_{10} exposure.

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.

Table S5. Sensitivity analyses: crude and adjusted ORs of neurodevelopmental disorders for twins born in Stockholm, by exposure to NO_x and PM_{10} in their 9th year of lives

Outcomes	Case	NO_x during 9th year of life OR[a] (95% CI)	NO_x during 9th year of life OR[b] (95% CI)	PM_{10} during 9th year of life OR[a] (95% CI)	PM_{10} during 9th year of life OR[b] (95% CI)
ASD					
ASD_{low}	109	0.75 (0.33,1.71)	0.93 (0.42,2.06)	0.93 (0.36,2.40)	1.14 (0.48,2.71)
ASD_{high}	33	1.07 (0.20,5.63)	1.30 (0.27, 6.21)	1.78 (0.33,9.66)	2.28 (0.50,10.35)
ASD_{DSM-IV}	47	1.11 (0.33, 3.73)	1.23 (0.38,3.97)	1.73 (0.49,6.17)	1.97 (0.58,6.76)
ADHD					
$ADHD_{low}$	328	0.94 (0.59,1.49)	1.14 (0.73,1.77)	1.08 (0.67,1.75)	1.27 (0.83,1.93)
$ADHD_{high}$	62	0.88 (0.28,2.78)	1.04 (0.33,3.21)	0.67 (0.27,1.66)	0.77 (0.33,1.79)
$ADHD_{DSM-IV}$	152	0.94 (0.50,1.76)	1.15 (0.62,2.15)	1.12 (0.57,2.20)	1.33 (0.73,2.41)
Any neurodevelopmental outcomes					
ASD or ADHD	355	0.93 (0.60, 1.44)	1.13 (0.74, 1.74)	1.07 (0.67, 1.70)	1.27 (0.84, 1.91)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at child's 9th year of life, parental education, family income, and neighborhood deprivation at child's 9th year of life.

Table S6. Sensitivity analyses: crude and adjusted ORs of ASD and ADHD comorbid with brain damage and chromosome abnormalities for twins born in Stockholm

Outcomes	Case*	NO_x during pregnancy		NO_x during infancy		PM_{10} during pregnancy		PM_{10} during infancy	
		OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
ASD									
ASD_{low}	44	0.56 (0.22,1.46)	0.42 (0.17,1.06)	0.72 (0.29,1.78)	0.50 (0.20,1.22)	0.65 (0.27,1.60)	0.57 (0.24,1.36)	0.90 (0.39,2.11)	0.76 (0.33,1.74)
ASD_{DSM-IV}	24	0.59 (0.19,1.78)	0.69 (0.28,1.68)	0.67 (0.23,1.98)	0.80 (0.41,1.54)	0.84 (0.27,2.56)	0.89 (0.43,1.87)	1.07 (0.35,3.27)	1.02 (0.51,2.01)
ADHD									
$ADHD_{low}$	48	0.49 (0.19,1.28)	0.55 (0.22,1.40)	0.65 (0.25,1.65)	0.65 (0.25,1.69)	0.55 (0.22,1.39)	0.68 (0.30,1.55)	0.67 (0.27,1.67)	0.71 (0.30,1.65)
$ADHD_{DSM-IV}$	34	0.43 (0.13,1.44)	0.50 (0.16,1.57)	0.59 (0.18,1.88)	0.61 (0.18,1.99)	0.53 (0.17,1.70)	0.59 (0.22,1.59)	0.67 (0.22,2.05)	0.64 (0.22,1.80)
Any neurodevelopmental outcomes									
ASD or ADHD	59	0.59 (0.26, 1.35)	0.55 (0.24, 1.23)	0.78 (0.35, 1.74)	0.66 (0.29, 1.51)	0.66 (0.30, 1.43)	0.71 (0.34, 1.48)	0.66 (0.30, 1.43)	0.71 (0.34, 1.48)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

*Cases comorbid with severe chromosome abnormality, malformations of the brain, epilepsy, cerebral palsy and other neurological disorders.

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.

Table S7. Sub-analysis: crude and adjusted ORs of neurodevelopmental disorders (using validated cut-off values) for twins (n=2,960) whose mothers answered the telephone interview

Outcomes	Case	NO_x during pregnancy		NO_x during infancy		PM_{10} during pregnancy		PM_{10} during infancy	
		OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)	OR[a] (95% CI)	OR[b] (95% CI)
ASD									
ASD_{low}	91	0.56 (0.22,1.41)	0.70 (0.28,1.75)	0.71 (0.34,1.48)	0.86 (0.41,1.79)	0.79 (0.33,1.89)	0.96 (0.44,2.09)	0.88 (0.46,1.66)	1.01 (0.57,1.77)
ASD_{high}	29	0.41 (0.13,1.26)	0.45 (0.13,1.54)	0.55 (0.20,1.55)	0.51 (0.18,1.45)	0.55 (0.19,1.58)	0.59 (0.21,1.64)	0.77 (0.27,2.18)	0.72 (0.28,1.87)
ASD_{DSM-IV}	41	0.33 (0.13,0.88)	0.36 (0.13,1.00)	0.48 (0.21,1.14)	0.48 (0.20,1.11)	0.57 (0.22,1.46)	0.56 (0.25,1.24)	0.83 (0.34,2.00)	0.76 (0.37,1.57)
ADHD									
$ADHD_{low}$	281	0.66 (0.41,1.06)	0.87 (0.54,1.39)	0.91 (0.60,1.38)	1.16 (0.76,1.78)	0.78 (0.50,1.20)	1.01 (0.66,1.53)	0.91 (0.62,1.33)	1.13 (0.78,1.65)
$ADHD_{high}$	53	0.35 (0.11,1.19)	0.50 (0.16,1.56)	0.60 (0.19,1.88)	0.79 (0.27,2.34)	0.38 (0.15,0.99)	0.55 (0.24,1.23)	0.56 (0.23,1.37)	0.72 (0.33,1.54)
$ADHD_{DSM-IV}$	132	0.49 (0.23,1.04)	0.63 (0.30,1.31)	0.75 (0.39,1.43)	1.00 (0.53,1.92)	0.71 (0.36,1.41)	0.89 (0.48,1.63)	0.85 (0.47,1.57)	1.11 (0.63,1.92)
Any neurodevelopmental outcomes									
ASD or ADHD	303	0.66 (0.43, 1.04)	0.85 (0.54, 1.33)	0.90 (0.61, 1.34)	1.13 (0.75, 1.70)	0.78 (0.52, 1.19)	0.99 (0.66, 1.48)	0.92 (0.64, 1.32)	1.12 (0.78, 1.61)

Definition of abbreviations: ASD=Autism Spectrum Disorders, ADHD= Attention Deficit/Hyperactivity Disorders, DSM-IV = Diagnostic and Statistical Manual of Mental Disorders (4th edition), OR=Odds Ratio, CI=Confidence Interval

[a] Estimates based on crude models.

[b] Models adjusted for parity, gender, maternal age during pregnancy, maternal smoking during pregnancy, maternal marital status at birth year, parental education, family income, and neighborhood deprivation at birth year.